

From biodiversity to nature deficiency in human health and disease

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Abstract Nature (biodiversity) loss is the loss or decline of the state of nature taking place in the wider environment. We present a novel concept, nature deficiency, referring to nature loss in the human body influencing health. Humans are connected with the natural environment and its microbes and biogenic chemicals through eating (drinking), breathing, and touching. The mental and sociocultural links to the environment are also strong. With medical and ecological research and guidelines, the diagnosis, prevention, and treatment of nature deficiency may become part of the clinical practice. Nature prescription is likely to find plausible forms in patient care and inspire preventive actions at the society level. Health professionals are in a key position to integrate public health promotion and environmental care.

Keywords: biodiversity, nature deficiency, nature loss, Finnish allergy programme, public health, nature prescription

Introduction

The negative impact of climate change and loss of biodiversity on human health has called for recognizing the positive effects of nature. Supporting health in an urban environment, green interventions and nature-based solutions have already become a commonplace.¹ Similarly, understanding the close relationship between the environmental and human microbiome has opened opportunities to promote health.

There is no consensus on the definition of *nature*.² The Oxford language dictionary defines it as the phenomena of the physical world collectively, including plants, animals, the landscape, and other features and products of the earth, as opposed to humans or human creations. The Millennium Ecosystem Assessment defined *ecosystem* as a dynamic complex of plant, animal, and microorganism communities and the nonliving environment interacting as a functional unit.³ The definition recognized humans as an integral part of ecosystems.

Here, we use the expression *humans and wider nature* to underline the fact that humans are part of nature although sometimes presented as a separate category.

Nature (biodiversity) loss is the loss or decline of the state of nature taking place in the wider environment.⁴ We present a novel concept, nature deficiency, referring to nature loss in the human body influencing health. In general, the connection of the human body as an ecosystem to wider ecosystems has weakened in the urban-like environment with modern lifestyle.

The *endogenous* nature deficiency is followed by microbial and chemical deprivation, impaired immunoregulatory circuits, low-grade inflammation, and disease risk. Humans also have strong mental and social links with the natural environment and may

suffer from *exogenous* nature deficiency, typically a lack of green spaces and outdoor activities in the housing environment or nearby.

Nature-deficit disorder was presented in 2005.⁵ It referred to children spending less time outdoors resulting in a wide range of behavioral problems. In the present paper, the concept of nature deficiency enlarges the perspective to biodiversity and biological ecosystem level.

With medical and environmental research and guidelines, the diagnosis, prevention, and treatment of nature deficiency may become part of the clinical practice. *Nature prescription* sounds vague today but is likely to find plausible forms in patient care and inspire preventive actions at the society level.

Biodiversity in medicine

In 1988, Edward O. Wilson and Frances M. Peter coined *biodiversity* in a book “calling attention to a most urgent global problem: the rapidly accelerating loss of plant and animal species to increasing human population pressure and the demands of economic development.”⁶ The book was based on a conference by the National Academy of Sciences and the Smithsonian Institution. It created a systematic framework for analyzing the problem and searching for solutions.

In 1992, the United Nations defined biological diversity as the variability among living organisms from all sources including interalia, terrestrial, marine, and other aquatic ecosystems as well as the ecological complexes of which they are part. This includes diversity within species, between species and ecosystems.⁷ The concept is not yet specific enough to gain full attention among

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citizens or health care professionals. Rockström and coworkers recently took up two different types of biodiversity: (i) largely intact natural ecosystems and (ii) the functional integrity of all ecosystems, including urban and agricultural ecosystems.⁸ The latter is certainly more directly related to the nature deficiency in the modern world.

In medicine, biodiversity was first used in bacteria and fungi⁹ and then as interaction between plant biodiversity and humans.¹⁰ Early papers proposed that biodiversity may be involved in human diseases, such as cancer¹¹ and infectious diseases.¹² However, among the 45,440 papers on biodiversity and disease, less than 50 were published before 2000 (retrieved on Medline December 16, 2023). In 2009, there were proposals that biodiversity may affect the human immune system.¹³

The alarming environmental changes, that is, the loss of biomass and biodiversity due to human activities, are now widely recognized^{14,15} (Fig. 1).¹⁶ *Nature (biodiversity) loss* includes, but is not limited to, the reduction of any aspect of biological diversity. The easy-to-understand concept has gained popularity and is currently widely used. However, it refers implicitly to the losses in wider nature around us and does not recognize the loss that is also taking place in the human body, that is, nature deficiency.

The idea that biodiversity loss leads to poor microbiota, immune dysfunction, and disease was introduced in 2011–2012.^{17,18} In 2013, the World Allergy Organization acknowledged *biodiversity hypothesis* as a position statement.¹⁹ It was reviewed in 2019 and implies that contact with a diverse natural environment enriches the human microbiome, promotes immune balance, and protects from allergy and inflammatory disorders.²⁰ This formulation of the hypothesis urgently calls for interventional studies and real-life testing.

The urbanized populations have alienated from natural environments and are suffering from nature deficiency. In a longitudinal study of pregnant women in Finland, the short-chain fatty acids in stool samples have markedly decreased over the past 20 years, indicating impoverished intestinal microbiota.²¹ The authors state that the reduction occurred in parallel with the decline of biodiversity in the living surroundings.

Allergies to pollen, animals, and food demonstrate the harmful immune response caused not by nature excess but by nature

deficiency, i.e. lack of protective factors. Exposure to potentially allergenic proteins in a biodiverse environment induces tolerance, while the exposure in “urban clean” environment may predispose to an inflammatory cascade in genetically inclined individuals. This was the case in the Finnish and Russian Karelia allergy disparity.²²

Diagnosis of nature deficiency

In medical practice, deficiency (eg, iron deficiency or hormonal deficiency) is often measured, diagnosed, and compensated by treatment. Nature deficiency should follow the same concept, requiring diagnosis and guidance for prevention and treatment.

A study sample of the skin or nasal microbiota can be easily obtained. The composition is then analyzed through amplicon sequencing and for taxonomic verification supplemented by metagenomic shotgun sequencing.²³ Testing may become rapid and affordable in the future. In stool samples, microbes and short-chain fatty acids are readily measurable and are surrogate markers of the gut microbiota.

Currently, there are no reference values for the richness or diversity of the microbiome, but different population surveys may identify critical imbalance. Comparison of the skin and nasal microbiota in Karelian young people has unmasked potential risk factors, such as the relative lack of genus *Acinetobacter*, for allergy and type 1 diabetes.^{24,25}

Immune tolerance for prevention and treatment

The ecosystem of human body is connected to the wider nature through eating (drinking), touching, and breathing. The immunologically relevant crosstalk between the ecosystems is mainly mediated by microbes and biogenic chemicals (BVOCs).²⁶ The immune system is a response to a biodiverse environment, which challenges innate immunity and boosts tolerance from cradle to grave. For example, early exposure to a microbe-rich farming environment protects from asthma and allergy by constantly shaping the innate immunity response.²⁷ The crosstalk is also mental and sociocultural, having measurable effects on health and wellbeing.²⁸

The Western type of diet and unnecessary antibiotic use (particularly in infancy) both reduce the diversity of the human microbiome.^{29,30} A plant-based diet supports health as many of its components have anti-inflammatory properties protecting

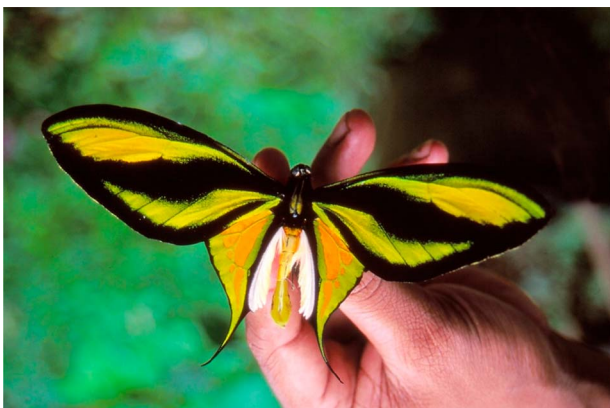


Figure 1. Even the most remote and pristine natural environments on earth are affected by human activities. The magnificent butterfly, the Paradise Birdwing (*Ornithoptera paradisea*, main subspecies *paradisea*), is most likely to be extinct because its habitat, the primary rain forest in Papua New Guinea, has been destroyed. The flourishing of butterflies as a marker of rich biodiversity and low allergy prevalence was introduced in 2009¹⁶ [photograph from a bred specimen.

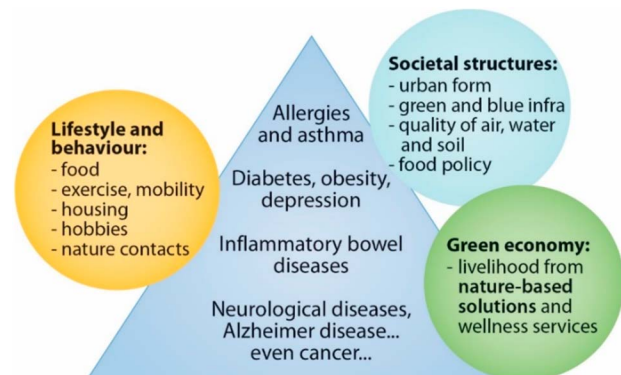


Figure 2. Natural elements must be taken back to everyday life to compensate for nature deficiency. The whole society is needed to strengthen protective factors for health and to mitigate risks (Furman E, Haahtela T. 2021, modified).

against noncommunicable diseases.^{31,32} Local food and self-produced fruits, vegetables, and roots maintain rich gut microbiota. Especially, the gut-brain axis is a hot topic at the moment, and associations between gut microbiota and mental disorders have been confirmed.³³

The touching of natural elements enriches the skin microbiota and influences immune regulation. In a controlled intervention study, daycare playgrounds were supplemented by soil blocks. After four weeks, the skin microbiota of the children in the intervention group was enriched with immunomodulatory effects.³⁴ Importantly, continuing the biodiversity intervention for up to two years sustained the microbiota.³⁵

In a placebo-controlled, double-blinded intervention, the playground sand was enriched with microbially diverse soil.³⁶ After two weeks, skin bacterial richness and diversity were higher in the intervention than in the placebo group, with immunomodulatory effects.

Pets (dog, cat) may support health.³⁷ A Danish group observed that their presence at home enriched the microbiota in bed dust and was associated with the infant airway microbiota.³⁸ However, as pets share the same environment and lifestyle as their owners, they may have the same disease risks.³⁹

Interpersonal, person-to-person relations modify the individual microbiomes. Recently, an extensive bacterial strain sharing was shown across individuals, with distinct mother-to-infant, intrahousehold, and intrapopulation transmission patterns.⁴⁰ Loneliness is both physical and mental!

Breathing air in natural environments provides biogenic volatile organic compounds (BVOCs) with health promoting effects.^{41,42} Identifying BVOCs in nature contacts and studying their immunological and clinical impact is an exciting field. In a recent Italian study of forest therapy, exposure to high concentrations of monoterpenes in the air relieved anxiety.⁴³ Urban green environments also provide favorable cardiovascular effects.⁴⁴ Data from Belgium have indicated that urban green spaces may protect against suicide mortality.⁴⁵ Mental effect is always involved in nature contacts. Even in office workers, virtual nature breaks have been shown to relieve stress.⁴⁶

Some urban populations may spend 90% of their time indoors. Improving indoor air by green walls enriched the skin microbiota of the employees and reduced the inflammatory cytokine IL-17A and increased the anti-inflammatory cytokine TGF- β 1.⁴⁷

Nature prescription

A nationwide public health campaign, the *Finnish Allergy Programme* (2008–2018), implemented the biodiversity hypothesis into practice by educating health care professionals to promote immune tolerance.⁴⁸ The lay public was targeted by a social media campaign. The favorable results of the real-world program have led to the controlled biodiversity interventions mentioned above.^{34–36}

Human microbiome and immune balance can be modified in a relatively short period of time, but only longer follow-ups can prove true symptom-modifying or disease preventive effects. For children, there is enough evidence to recommend safe contacts with a biologically rich environment.⁴⁸ Nature contacts, preferably with physical activity, also help to boost immune regulation in the elderly, most important for today's aging populations in Europe and elsewhere.

In the treatment of noncommunicable diseases, enhancing immune tolerance is increasingly favored. Managing allergy, for

example, by oral immunotherapy, against pollen, mite, and food is an example.⁴⁹

In medical practice, modifying the gut microbiota to prevent and treat diarrhea and irritable bowel syndrome is already a commonplace. Probiotics are widely recommended, although a recent systematic review was unable to draw consistent conclusions regarding their effects on the gut microbiota in adults.⁵⁰

Faecal microbiota transplantation is a current way of treating severe diarrhea caused by *Clostridioides difficile*. Studies treating inflammatory bowel diseases⁵¹ and even preventing Alzheimer are ongoing.⁵²

Compensating for nature deficiency aims to strengthen the immune system. It can work as an adjuvant therapy or even as a main therapy in milder cases like occasional allergy symptoms. Furthermore, exposure to natural environment may reduce the need for long-term medication, for example, drugs for asthma, hypertension, and psychic disorders.⁵³

Health professionals usually work on a “patient-by-patient” basis. With joined medical and environmental research and guidelines concerning everyday life, the prevention and treatment of nature deficiency may find an increasing role in the clinical practice.⁵⁴

Real-world implementation

Climate change intertwined with biodiversity loss represents a major threat for humanity, directly by its effects on individuals and indirectly by its major political impact. For example, the survival of many African populations is under immediate threat.

In most societies, the COVID-19 pandemic indicated the precedence of human health and health safety.⁵⁵ This is also a main priority in the concept of *Planetary Health* defined as “health of human civilization and the state of the natural systems on which it depends.”⁵⁶ The older concept of *One Health* was recently updated to mean an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems.⁵⁷

Climate change is widely understood by citizens, but very few—and even fewer policy makers—are aware of biodiversity (nature) loss and its impact. Integrating climate change, biodiversity loss, and planetary health to a conceptual package would enable a more ambitious mitigation strategy than climate change only. This must start at the citizen level with acceptable strategies, which are also economically plausible for policy makers.

Health professionals are in a key position to prevent and treat nature deficiency in their patients. They can also help to integrate public health and environmental care to reach the vital aim of planetary health.^{58–60}

The first experiences of the local *Health and Environment Programme* (2022–2032) in the city of Lahti, EU Green Capital 2021, are encouraging.⁶¹ A *planetary health physician* considers health care and environment stakeholders to improve the citizens' diet, physical exercise, mobility, housing environment, and contacts with wider nature.⁶² The imperative actions are presented in Figure 2.

Finally, implementation should be based on evidence. Our knowledge on the close connection between nature and human health is still in its infancy. We need to incorporate studies on the various forms of nature deficiency as a priority in research programs. Modern tools, such as digital health and artificial intelligence, may prove to be of major value in finding practical solutions.

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